

57. **(Thrice Amended)** A method of stimulating a population of undifferentiated mammalian mesodermally derived cells to undergo hematopoiesis, comprising contacting the cells with an amount of a hedgehog compound effective to stimulate the cells to undergo hematopoiesis, wherein the hedgehog compound comprises a polypeptide sequence at least 80% identical to a sequence selected from SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, or a fragment thereof, which polypeptide sequence is functionally equivalent to a naturally occurring hedgehog protein, binds to *patched* and induces cells to undergo hematopoiesis.

58. **(Reiterated)** A method according to claim 57, wherein the hedgehog compound is an Indian hedgehog, Desert hedgehog, or Sonic hedgehog protein or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis.

59. **(Reiterated)** A method according to claim 57, wherein the hedgehog compound is an Indian hedgehog protein or fragment thereof which binds to *patched*.

60. **(Twice Amended)** A method according to claim 82 80, wherein the TGF- $\beta$  polypeptide is a bone morphogenic protein.

61. **(Reiterated)** A method according to claim 60, wherein the bone morphogenic protein is BMP-2, BMP-4, BMP-6, or BMP-7.

62. **(Reiterated)** A method according to claim 57, further comprising maintaining the cell population in vitro in a culture medium, and wherein contacting the cells with a hedgehog compound includes contacting the cells with a culture medium comprising the hedgehog compound.

63. **(Reiterated)** A method according to claim 57, wherein the undifferentiated mesodermally derived cells are hematopoietic stem cells.

64. **(Reiterated)** A method according to claim 63, wherein the hematopoietic stem cells are selected from cord blood cells, fetal liver cells, and peripheral blood cells.

65. **(Reiterated)** A method according to claim 63, wherein the hematopoietic stem cells are obtained from adult bone marrow cells.
66. **(Reiterated)** A method according to claim 57, wherein the cells are progenitor cells obtained from an adult human.
67. **(Reiterated)** A method according to claim 57, wherein the cells comprise embryonic tissue.
68. **(Reiterated)** A method according to claim 57, wherein the cells comprise an embryonic explant culture.
69. **(Reiterated)** A method according to claim 68, wherein the embryonic explant culture is a blastocyst.
70. **(Reiterated)** A method according to claim 57, wherein the cells are hematopoietic stem cells within the bone marrow of an animal.
71. **(Reiterated)** A method according to claim 57, wherein the cells are hematopoietic stem cells present in the animal in at least one of bone marrow, cord blood cells, fetal liver cells and peripheral blood cells.
72. **(Reiterated)** A method according to claim 70, wherein contacting the stem cells with the hedgehog compound includes administering an effective dose of the compound to the animal by any of oral, intradermal, subcutaneous, transmucosal, intramuscular, or intravenous routes.
73. **(Reiterated)** A method according to claim 82, wherein the TGF- $\beta$  polypeptide enhances the stimulation of hematopoiesis of the cells by more than the amount of stimulation of hematopoiesis resulting from administration of an identical amount of the TGF- $\beta$  polypeptide in the absence of the hedgehog compound.

82. **(Reiterated)** A method according to claim 57, further comprising contacting the cells with a TGF- $\beta$  polypeptide.

83. **(Twice Amended)** A method of stimulating hematopoiesis in an animal, comprising administering to the animal an effective amount of a hedgehog compound comprising a polypeptide sequence at least 80% identical to a sequence selected from SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, or a fragment thereof, which polypeptide sequence is functionally equivalent to a naturally occurring hedgehog protein, binds to *patched* and induces cells to undergo hematopoiesis.

84. **(Reiterated)** A method according to claim 83, wherein the hedgehog compound is an Indian hedgehog, Desert hedgehog, or Sonic hedgehog protein or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis.

85. **(Reiterated)** A method according to claim 83, further comprising contacting the cells with a TGF- $\beta$  polypeptide.

86. **(Reiterated)** A method according to claim 85, wherein the TGF- $\beta$  polypeptide is a bone morphogenic protein.

87. **(Reiterated)** A method according to claim 86, wherein the bone morphogenic protein is selected from BMP-2, BMP-4, BMP-6, and BMP-7.

88. **(Twice Amended)** A method of stimulating a population of undifferentiated mammalian mesodermally derived cells to undergo hematopoiesis, comprising contacting the cells with an effective amount of a hedgehog compound comprising a polypeptide sequence of SEQ ID NO: 41, SEQ ID NO: 42, or a fragment thereof, which polypeptide sequence is functionally equivalent to a naturally occurring hedgehog protein, ~~which~~ binds to *patched* and induces cells to undergo hematopoiesis.

89. **(Reiterated)** A method according to claim 88, wherein the undifferentiated mesodermal-derived cells are a population of hematopoietic stem cells.

90. **(Reiterated)** A method according to claim 89, wherein the hematopoietic stem cells are selected from cord blood cells, fetal liver cells, and peripheral blood cells.
91. **(Reiterated)** A method according to claim 89, wherein the cells are human progenitor cells.
92. **(Reiterated)** A method according to claim 89, wherein the cells are hematopoietic stem cells within the bone marrow of the animal.
93. **(Reiterated)** A method according to claim 89, wherein the cells are hematopoietic stem cells present in the animal in at least one of bone marrow, cord blood cells, fetal liver cells and peripheral blood cells.
94. **(Reiterated)** A method according to claim 83, wherein an effective dose of the hedgehog compound is administered to the animal by any of oral, intradermal, subcutaneous, transmucosal, intramuscular, or intravenous routes.
95. **(Twice Amended)** A method of stimulating hematopoiesis in an animal, comprising administering to the animal an effective amount of a hedgehog compound comprising a polypeptide sequence of SEQ ID NO: 41, SEQ ID NO: 42, or a fragment thereof, which polypeptide sequence is functionally equivalent to a naturally occurring hedgehog protein, which binds to *patched* and induces cells to undergo hematopoiesis.
96. **(Twice Amended)** A method of stimulating a population of undifferentiated mammalian mesodermally derived cells to undergo hematopoiesis, comprising contacting the cells with an amount of a hedgehog compound effective to stimulate the cells to undergo hematopoiesis, wherein the hedgehog compound comprises a polypeptide sequence encoded by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID Nos. 27-33, which polypeptide sequence is functionally equivalent to a naturally occurring hedgehog protein, binds to *patched* and induces cells to undergo hematopoiesis.

97. **(Reiterated)** A method according to claim 96, wherein the hedgehog compound is an Indian hedgehog, Desert hedgehog, or Sonic hedgehog protein or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis.
98. **(Reiterated)** A method according to claim 96, wherein the hedgehog compound is an Indian hedgehog protein or fragment thereof which binds to *patched*.
99. **(Reiterated)** A method according to claim 96, further comprising contacting the cells with a TGF- $\beta$  polypeptide.
100. **(Reiterated)** A method according to claim 99, wherein the TGF- $\beta$  polypeptide is a bone morphogenic protein.
101. **(Reiterated)** A method according to claim 100, wherein the bone morphogenic protein is BMP-2, BMP-4, BMP-6, or BMP-7.
102. **(Reiterated)** A method according to claim 96, further comprising maintaining the cell population in vitro in a culture medium, and wherein contacting the cells with a hedgehog compound includes contacting the cells with a culture medium comprising the hedgehog compound.
103. **(Reiterated)** A method according to claim 96, wherein the undifferentiated mesodermally derived cells are hematopoietic stem cells.
104. **(Reiterated)** A method according to claim 103, wherein the hematopoietic stem cells are selected from cord blood cells, fetal liver cells, and peripheral blood cells.
105. **(Reiterated)** A method according to claim 103, wherein the hematopoietic stem cells are obtained from adult bone marrow cells.
106. **(Reiterated)** A method according to claim 96, wherein the cells are progenitor cells obtained from an adult human.

107. **(Reiterated)** A method according to claim 96, wherein the cells comprise embryonic tissue.
108. **(Reiterated)** A method according to claim 96, wherein the cells comprise an embryonic explant culture.
109. **(Reiterated)** A method according to claim 108, wherein the embryonic explant culture is a blastocyst.
110. **(Reiterated)** A method according to claim 96, wherein the cells are hematopoietic stem cells within the bone marrow of an animal.
111. **(Reiterated)** A method according to claim 96, wherein the cells are hematopoietic stem cells present in the animal in at least one of bone marrow, cord blood cells, fetal liver cells and peripheral blood cells.
112. **(Reiterated)** A method according to claim 111, wherein contacting the stem cells with the hedgehog compound includes administering an effective dose of the compound to the animal by any of oral, intradermal, subcutaneous, transmucosal, intramuscular, or intravenous routes.
113. **(Reiterated)** A method according to claim 99, wherein the TGF- $\beta$  polypeptide enhances the stimulation of hematopoiesis of the cells by more than the amount of stimulation of hematopoiesis resulting from administration of an identical amount of the TGF- $\beta$  polypeptide in the absence of the hedgehog compound.

#### **REMARKS**

Claims 57-73 and 82-113 constitute the pending claims in the present application. Claims 74 and 75, if considered to be pending, are hereby cancelled. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.